16.0 Scientific Abstract

The HIV-1 Rev protein is encoded by a fully spliced viral mRNA synthesized early in virus infection and required for productive HIV replication (23). Rev facilitates the cytoplasmic appearance of unspliced viral mRNAs and plays a role in the regulation of virus latency (24,25). Mutations in a well-conserved leucine rich domain of Rev give rise to a defective protein that acts as a transdominant inhibitor of HIV replication, which could provide a potential anti-HIV therapy. In this study, we will evaluate the efficacy of intracellular inhibition of HIV infection with a with mutant form of Rev, M10. We will introduce the rev M10 gene into peripheral blood $CD4^+$ T cells. $CD4^+$ cells will be genetically modified in patients using either (a.) a retroviral vector or (b.) a non-viral vector. In each case, a control vector identical to the Rev M10 expression vector but with a frameshift that inactivates gene expression will be used to transduce a parallel population of $CD4^+$ cells. These cells will be returned to the patient, and the survival of the cells in each group compared by limiting dilution PCR. In this way, we will determine whether Rev M10 can prolong the survival of $CD4^{\oplus}$ cells in AIDS patients, thus conferring protection against HIV infection.